REMARKS/ARGUMENTS

With this amendment, claims 23-40 are pending. Claims 31-38 are cancelled without prejudice to subsequent revival. New claims 39 and 40 are added. For convenience, the Examiner's rejections are addressed in the order presented in a January 29, 2004 Office Action.

I. Status of the claims

Claims 31-38 are cancelled without prejudice to subsequent revival. Claim 23, is amended to recite an isolated polynucleotide fragment of the methylthioadenosine phosphorylase (MTAse) protein coding domain of SEQ ID NO:1 comprising a specific sequence, *i.e.*, nucleotides 2838-2876. Support for an MTAse protein coding domain of an MTAse polynucleotide is found throughout the specification, for example, at page 4, lines 8-11. Support for a fragment of an MTAse polynucleotide is found throughout the specification, for example, at page 13, line 26 through page 14, line 2 and page 14, lines 10-15. Similar amendments of claims 25, 27, and 29 are submitted, and the same passages are cited for support. These amendments add no new matter.

Claims 24, 26, 28, and 30 are amended to correct the antecedent basis by which they depend on amended claims 23, 25, 27, and 29. These amendments add no new matter.

New claim 39 is added and depends from claims 23, 25, 27, and 29. Claim 39 recites that the isolated polynucleotide fragments are labeled. Support for this amendment is found throughout the specification, for example, at for example, at page 11 line 16 through page 12, line 12. This amendment adds no new matter.

New claim 40 is added and depends from claims 23, 25, 27, and 29. Claim 40 recites that the isolated polynucleotide fragments are used to determine MTAse deficiency in a biological sample. Support for this amendment is found throughout the specification, for example, at for example, at page 4, lines 8-11 and at original claim 1. Support for a biological sample is found throughout the specification, for example, at page 7, lines 12-16. This amendment adds no new matter.

II. Priority

According to the Office Action, the claims are awarded priority of March 26, 1997 for the invention of a nucleic acid sequence having SEQ ID NO:1, which encodes full length MTAse. The full length genomic MTAse sequence was disclosed in a continuation-in-part application, USSN 08/827,342 (the '342 application), filed March 26, 1997. Because the application with the earliest filing date to which priority is claimed [*i.e.*, USSN 08/176,855, (the '855 application) filed December 29, 1993] disclosed a partial genomic MTAse sequence, the Office Action appears to assert that the priority claim to the '855 application should be denied for all pending claims. Applicants respectfully traverse the priority decision. In addition, Applicants respectfully assert that any material added to the '342 CIP application cannot be characterized as new matter, because the application was correctly identified as a continuation-in-part application at the time of filing.

The pending claims are not directed to nucleic acids that encode a full length MTAse protein. Rather, the claims are directed to nucleic acid probes, *e.g.*, fragments of the protein coding domain of SEQ ID NO:1 (*i.e.*, genomic MTAse nucleic acids, including exons), that can be used to detect a deletion of the chromosomal MTAse gene, and thus used to diagnose malignancy or to identify cancer patients that will respond to a targeted chemotherapy regime. The claimed nucleic acids do not encode a full-length MTAse protein because they are fragments of the protein coding domain of SEQ ID NO:1. Applicants were the first to discover a diagnostic use for fragments of the protein coding domain of the MTAse gene and accordingly disclosed nucleic acids with the necessary properties in the '855 application.

The present application has the same disclosure as the '342 CIP application and the priority date of individual claims is appropriately determined based on the earliest disclosure of the subject matter, *i.e.*, in the 1993 '855 application or in the 1997 '342 CIP application. The nucleic acids of claims 25-30 were disclosed in the '855 application and in each of the applications in the priority chain down to the present application. As explained in the previous response, in both the priority '855 application and the current application, exons are disclosed in Figure 1 as underlined sequences. Exon 6 is currently claimed as nucleotides 1764-1953 of SEQ ID NO:1, and in the priority '855 application was disclosed as nucleotides 964-1203 of SEQ ID

NO:1, *i.e.*, Figure 1 of the priority '855 application. Exon 7 is currently claimed as nucleotides 2426-2548 of SEQ ID NO:1, and in the priority '855 application was disclosed as nucleotides 1640-1762 of SEQ ID NO:1, *i.e.*, Figure 1 of the priority '855 application. Exon 8 is currently claimed as nucleotides 2838-2876 of SEQ ID NO:1, and in the priority '855 application was disclosed as nucleotides 2272-2310 of SEQ ID NO:1, *i.e.*, Figure 1 of the priority '855 application. Thus, claims 25-30 are entitled to the benefit of the December 29, 1993 filing date.

III. New grounds of rejection under 35 U.S.C. §112, first paragraph, written description

Claims 23-38 are newly rejected under 35 U.S.C. §112, first paragraph for alleged lack of written description. According to the Office Action, the claims contain subject matter that was not described in the specification in a way to convey to one of skill that the inventors had possession of the claimed invention at the time of filing.

Specifically, the Office Action alleges that the specification lacks support for an isolated polynucleotide that hybridizes under stringent conditions to a nucleotide sequence less than 500 basepairs long, comprising particular nucleotides of SEQ ID NO:1. In addition, the Office Action alleges that the specification fails to support claims to probes or nucleic acids consisting of exon sequences. To the extent the rejection applies to the amended claims, Applicants respectfully traverse.

In order to expedite prosecution, the independent claims (*i.e.*, claims 23, 25, 27, and 29) now recite an "isolated polynucleotide fragment of the methylthioadenosine phosphorylase (MTAse) protein coding domain of SEQ ID NO:1 comprising nucleotides . . . [recitation of specific nucleotides for each independent claim] of SEQ ID NO:1 or its complement." Descriptive support for an MTAse protein coding domain of SEQ ID NO:1 is found *e.g.* at page 4, lines 8-11 of the present application and at page 4, lines 8-11 of the priority '855 application, which recites in part, "a polynucleotide inside the MTAse protein coding domain of the mammal's genome . . ." The genomic MTAse sequence and claimed exons (*i.e.* portions of the protein coding domain) are found in Figure 1 and SEQ ID NO:1 of both applications, see, *e.g.* above. Descriptive support for a fragment of an MTAse polynucleotide is found throughout both specifications, for example, at page 13, lines 26 through page 14, line 2

and at page 14, lines 10-15 of the present application; and at page 13, lines 22-24 and page 14, lines 6-11 of the priority '855 application. A fragment of a molecule, such as any polynucleotide of the invention, is defined as including "any nucleotide subset of the molecule." Thus, the MTAse protein coding domains of SEQ ID NO:1 are described in the specification, as are fragments of that sequence, and the description would lead one of skill to conclude that the inventors had possession of the invention at the time of filing the application.

The Office Action appears to assert a requirement for language expressly describing particular subsequences of the MTAse nucleic acid sequence. Applicants respectfully remind the Examiner that there is no *in haec verba* requirement for amendment of claims, so long as new claim limitations are "supported in the specification through express, implicit, or inherent disclosure." MPEP 2163(I)(B). Even if the Examiner continues to assert a lack of explicit description of particular fragments of the MTAse coding domains of disclosed polynucleotides, that subject matter is inherently described in the application. The exons disclosed in Figure 1 of the present application and the priority '855 application are inherently fragments of an MTAse protein coding domain of SEQ ID NO:1. According to the MPEP, an application that discloses an inherent function or property of claimed subject matter necessarily discloses the function or property, even though nothing is explicitly stated concerning the inherent function or property. MPEP 2163.07(A). Thus, the priority '855 application and the present application provide descriptive support for the claimed polynucleotide fragments.

According to the Office Action, there is no support for probes or for nucleic acids consisting of MTAse exons. This is incorrect and Applicants continue to assert that rejected claims 26, 28, and 30 should be allowed. Nucleic acids that consist of exons, *i.e.*, fragments of the MTAse coding domain of SEQ ID NO:1, are specifically described in Figure 1 of the pending Application, and were also described in Figure 1 of the priority '855 application. As such, nucleic acids that consist of exons meet the written description requirement and claims directed to that subject matter should be allowed.

Thus, based on the disclosure of the specification, one of skill would recognize that the inventors had possession of the claimed invention at the time of filing. In view of the

above amendments and remarks, Applicants respectfully request that the new rejections under 35 U.S.C. §112, first paragraph be withdrawn.

IV. Maintained grounds of rejection under 35 U.S.C. §112, first paragraph, written description

The previous rejection of claims 23, 25, 27, 29, 31, 33, 35, and 37 under 35 U.S.C. §112, first paragraph for alleged lack of written description is maintained, because of the use of hybridization language. In order to expedite prosecution, the claims are amended to remove hybridization language. In view of the amendments and arguments within this response, Applicants respectfully request withdrawal of the maintained rejections under 35 U.S.C. §112, first paragraph.

V. Rejections for double patenting

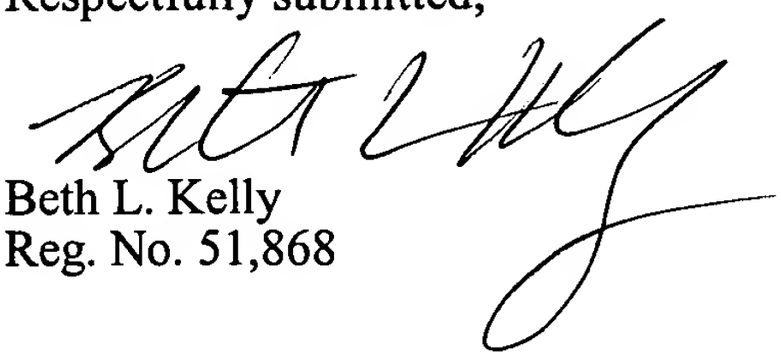
Claims 23-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 9 of U.S. Patent No. 5,942,393. In order to expedite prosecution, if the double patenting rejection is maintained for the amended claims, Applicants will file a terminal disclaimer to overcome the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments

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